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Award Number: DAMD17-98-IA-8002

TITLE: A Dietary Strategy to Maximize Bone Mass in United States
Naval Academy Midshipmen

PRINCIPAL INVESTIGATOR: Mona Calvo, Ph.D.

CONTRACTING ORGANIZATION: U.S. Food and Drug Administration
Rockville, Maryland 20852

REPORT DATE: October 1999

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

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REPORT DOCUMENTATION PAGE

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13. ABSTRACT (Maximum 200 Words)

The overall objective of this research is to develop dietary methods to increase bone mass in young men and women in order to reduce the incidence of stress fractures during physical training and the incidence of osteoporotic fracture later in life. The study evaluates the efficacy and safety of two different types of dietary interventions to promote gain in bone mass at several skeletal sites in young Naval Academy Midshipmen. The dietary interventions optimize different nutritional factors, not just calcium intake, and enable us to examine the effect of maximizing all the nutrients essential for both bone matrix formation and bone mineralization under the conditions of usual dietary intake at the Naval Academy. The youngest Midshipmen were recruited because they have the greatest potential for bone accretion, consequently recruitment was coordinated with the initiation of the class of 2003. The beginning phase of recruitment and baseline measurement of bone mineral density parameters and estimates of dietary intake that are needed to randomize the subjects to treatment groups started in July 1999. To date, we have recruited and scanned approximately 100 Midshipmen. The two year dietary intervention phase will start in early 2000. Midshipmen will be randomized to groups consuming daily either a calcium supplement or a placebo and either a fortified protein and energy bar or its placebo. Contracts for the development and production of the two different dietary supplements and their respective placebos are under negotiation with the U.S. Army Combat Feeding Center, Natick Soldier Center, SBCCOM, Natick, MA.

14. SUBJECT TERMS: Peak Bone Mass; Calcium Supplements; Food-based Vitamin and Trace Mineral Protein Supplement; Bone Mineral Density; Bone Turnover Markers; Parathyroid Hormone; and Insulin-like-

15. NUMBER OF PAGES
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298-102

DTIC QUALITY INSPECTED 1

FOREWORD

Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the U.S. Army.

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_____ Citations of commercial organizations and trade names in this report do not constitute an official Department of Army endorsement or approval of the products or services of these organizations.

_____ In conducting research using animals, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and use of Laboratory Animals of the Institute of Laboratory Resources, national Research Council (NIH Publication No. 86-23, Revised 1985).

_____ For the protection of human subjects, the investigator(s) adhered to policies of applicable Federal Law 45 CFR 46.

_____ In conducting research utilizing recombinant DNA technology, the investigator(s) adhered to current guidelines promulgated by the National Institutes of Health.

_____ In the conduct of research utilizing recombinant DNA, the investigator(s) adhered to the NIH Guidelines for Research Involving Recombinant DNA Molecules.

_____ In the conduct of research involving hazardous organisms, the investigator(s) adhered to the CDC-NIH Guide for Biosafety in Microbiological and Biomedical Laboratories.

 10-26-99
PI - Signature Date

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INTRODUCTION

The overall objective of this study is to optimize nutritional factors to maximize gain in bone mass during early adulthood, which is a cost-effective approach to reduce stress fractures during physical training and the risk of osteoporotic fracture later in life. The risk of bone fracture is largely dependent on the peak bone mass achieved at skeletal maturity and early adulthood is considered the last window of opportunity to maximize gain in bone mass. This study evaluates the safety and efficacy of two types of dietary supplements, either by themselves or in combination, to promote gain in bone mass at several skeletal sites in young Naval Academy Midshipmen. We examine the effect of optimizing either calcium intake alone or in combination with adequate intakes of other nutrients essential for building bone in young adults. Many of these other essential nutrients are limited in the typical diets of teens and young adults. We will compare gains in bone mass at several skeletal sites in four groups of male and female Midshipmen fed different combinations of calcium supplements or placebo tablets, both with or without a fortified protein supplement, all of which are consumed daily for two years. If optimizing the diet is effective, we would anticipate greater changes in bone mass for groups consuming any combination of the dietary supplements compared to the changes observed in the placebo/placebo-fed Midshipmen consuming only their usual dietary intake at the Naval Academy. It is important to study the youngest Midshipmen, because they have the greatest overall potential for increasing bone accretion through diet and exercise. Consequently, we waited to recruit subjects from the class of 2003 who entered the Naval Academy in July 1999. The efficacy of these two dietary interventions to promote gain in bone will be assessed by periodically monitoring changes in bone mineral content and bone mineral density of the spine, femoral neck, distal tibia, and whole body measured by dual energy X-ray absorptiometry. Monitoring changes in calcitropic hormones, insulin-like growth factor, and in resorption and formation markers of bone turnover, as well as changes in urinary loss of calcium over the two-year study will provide insight into the possible mechanisms through which the two dietary interventions may influence gain in bone mass.

Body

Tasks listed in the Approved Statement of Work that are pertinent to the Annual Report covering research for the period of September 30, 1998 to September 29, 1999 are as follows:

- Task 1** Month 1-8, Negotiate contracts for test products and analyses, begin recruitment of men and women with testing and baseline measures needed to stratify to treatment. Secure GLP procedures for manufacture of test supplements; assure the products meet FDA specifications. ORISE personnel initiated on study.
- Task 2** Months 9 -12, Stratification of volunteers to treatment and treatment initiation.

Here, we describe the research accomplishments, progress, and various problems associated with each of the elements in Tasks 1 and 2 of the approved Statement of Work .

Task 1:

Month 1-8, Negotiate contracts for test products and analyses.

Because the anticipated cost of the fortified protein supplement exceeded \$25,000, the FDA was obligated to fully and openly compete this contract concerning the development and manufacture of the fortified protein supplement and its placebo. We also needed to avoid demonstration of preferential treatment to any manufacturer, since the Center for Food Safety and Applied Nutrition is FDA's main regulatory center for food and dietary supplements. Evidence of our efforts to place this contract in full and open competition are shown by the first three pages (out of a total of 61) for the *Solicitation, Offer and Award* issued by FDA (Appendices, pages 11-13). No offers were received, even after a 30 day extension of the August 9, 1999 due date. A *Request for Quotation* was issued July 29, 1999 by the FDA Contracts Operation Branch for the calcium citrate and placebo contracts as shown by the first page (out of 6) on pages 14 and 15 of the Appendices. Again, no bids for the supply of the calcium supplements and placebo were received.

At this time, FDA was free to negotiate with the Combat Feeding Program at Natick Soldier Center to procure both the fortified protein supplement and placebo and the

calcium supplements and placebo tablets. The FDA offered the *Inter Agency Agreement* shown on pages 16 to 19 of the Appendices in order to commit funds for this procurement before the end of FY99. Due to problems with end of year acceptance of funds, we were unsuccessful in establishing this IAG for FY99, but both Natick and FDA are eager to resume negotiations for FY2000. However, we encountered problems with the budget since the estimated cost of both types of dietary supplements and placebos for the proposed total number of subjects for two years far exceeded the total approved budget of \$225,000. We have requested approval of changes in our study design that will allow us to cover the estimated additional costs based on Natick's estimates. These issues are raised in our October 21, 1999 *Memorandum Requesting Approval of Changes in Study Design and Request for Additional Funds* shown in Appendices pages 20 to 22.

As presented in the *Memorandum*, we propose a change in the study design that reduces the subject number in each group from 35 to 30, without diminishing the power of the study to detect differences in bone mass. This would lower the estimated cost of the bars, but would still require additional funds of approximately \$45,000, since total estimated cost for 240 subjects over two years is \$270,000.

With respect to negotiating contracts for the various analyses, we have decided to contract in-house with FDA's Center for Food Safety and Applied Nutrition's Clinical Chemistry Unit located in the same laboratory facilities as the Principal Investigator's laboratory. This convenient in-house arrangement does not require contractual agreement and is currently in place (pages 23 to 25 of the Appendices). Specialized analyses for insulin-like growth factor and osteocalcin and N-telopeptide of type 1 collagen of bone will be carried-out through sole source contracts to be negotiated for FY2000 with Dr Gundberg at Yale and Dr. Rosen at the University of Maine.

To fund a third-party arrangement for the determination of bone mineral density scans that would be supervised by the Co-Principal Investigator, Dr. David Armstrong, the FDA offered an *Inter Agency Agreement* to the Office of Naval Research who in turn was to pass these funds to the Henry Jackson Foundation for Military Research (the third party through which Dr. Armstrong is employed). This *Inter Agency Agreement* is shown in the Appendices on page 26 to 29. The departure of CDR Douglas Forcino, Program Officer for the Office of Naval Research and our liaison for the contract, precipitated a great deal of confusion which led to the ultimate rejection of the IAG by the Navy Contract Specialists, at the end of FY99. In the last month, we clarified this many layered misunderstanding and the Office of Naval Research is now willing to accept the IAG, if FDA will re-issue it. We are currently in the process of preparing this IAG.

Begin recruitment of men and women with testing and baseline measures needed to stratify to treatment.

We began recruiting male and female Midshipmen with the initiation of the class of 2003 in July 1999. To date approximately 100 Midshipmen have given written consent and have been scanned for bone mineral density at specific skeletal sites. Ultrasound measures were not taken due to the lack of availability of a dedicated sonometer located at the Naval Academy. There is no need to amend the study design due to the absence of this measurement, because the ultrasound parameters were not approved for funding in the original proposal. An ultimate goal of 240 Naval Midshipmen must be recruited with our modified study design, if our proposed modifications are approved. While there are no anticipated problems in recruiting the needed number of men (120), we are already experiencing problems in recruiting the needed number of female Midshipmen from the class of 2003. Fewer women chose to attend the Naval Academy this year and of those who entered in July, approximately thirty have dropped out, giving us a small population of about 150 women from which to meet our original goal of 140 female participants. This means that we would have to successfully recruit over 80% of the women in the class of 2003. We will know in the next month approximately how many more women we need to meet our goal of 120.

One possible consideration would be to recruit from among the youngest female Midshipmen in the class of 2002, who would be on average 19+ years of age and in their third semester at the Naval Academy. We anticipate the need to recruit 30 to 50 female Midshipmen from the class of 2002, but we would wait for approval before making this change.

Another option would be to proceed with the current insufficient number of women, but recruit the remainder from the incoming class of 2004. This would necessitate waiting an entire year to randomize the group to different treatments. This approach has other complications in that the supplements have a two-year shelf life when stored at -20°C and to save cost they are all produced in one large batch and then refrigerated until needed. In their last year of study, female Midshipmen recruited from the class of 2004 would have to consume supplements and placebos that exceeded the shelf life. We, therefore, need guidance and approval concerning the action to take in order to recruit the needed number of female Midshipmen.

Secure GLP procedures for manufacture of test supplements; assure the products meet FDA specifications.

These measures and procedures are built into the contract with Natick and are described as the quality control and assessment for specific nutrient levels that provide evidence that the products meet the specifications needed by FDA.

ORISE personnel initiated on study. A Registered Dietician with over 10 years of clinical experience, Sheila Mackertich, R.D., was recruited through the ORISE program in FY99. At this time, she is assessing dietary intake through 3-day food records and collecting 24-hour urine on all those Midshipmen who have had their baseline bone mineral density measured.

Task 2

Months 9 -12, Stratification of volunteers to treatment and treatment initiation.

We have not completed baseline measurements on the total number of subjects judged by our power estimates to be sufficient to detect differences in bone mass for specific treatment groups. At this time, we are not ready to stratify our subjects into treatment groups which places us approximately four months behind schedule. While this delay may not appear to be significant, there is need for concern, because the Midshipmen will be leaving in May for three months of summer sea duty. It is important that we introduce the dietary intervention in March of 2000 to sufficiently acclimate the Midshipmen to the habit of nightly eating the fortified protein bars and pills. We are making a concerted effort to complete all needed baseline measurements by February 2000 in order to stratify the Midshipmen to treatments and to initiate the dietary intervention by March.

Key Research Accomplishments

- There are no key research accomplishments to date as the work is in the baseline phase of data collection in preparation for the introduction of the dietary interventions.

Reportable Outcomes

- In this preliminary phase, there are no reportable outcomes at this time; however, it is our intention to prepare an abstract reporting aspects of the baseline measures when we have completed recruitment and measurement of the 240 subjects.
- We are preparing a report for the concerned physicians at the National Naval Medical Center, located at the Naval Academy, documenting self-reported use of dietary supplements including regular consumption of ergogenic aids to enhance physical performance by the randomly screened incoming class of 2003. This information was gathered during the early recruiting phase of the study.

Conclusions

- No conclusions can be made in this early stage of experimentation.

References

- There are no reportable references at this time.

Appendices

<u>Documents</u>	<u>Pages</u>
• Solicitation, Offer, and Award -----	11 -- 13
• Request for Quotation -----	14 -- 15
• Inter Agency Agreement for Dietary Supplements -----	16 -- 19
• Memorandum Requesting Approval of Changes in Study Design And Request for Additional Funds-----	20 -- 22
• Cost Estimates for Clinical Chemistry Unit Analyses -----	23-- 25
• Inter Agency Agreement for Bone Mineral Density Determinations -----	26 -- 29

SOLICITATION, OFFER AND AWARD		1. THIS CONTRACT IS A RATED ORDER UNDER DPAS (15 CFR 350)		RATING		PAGE OF PAGES	
2. CONTRACT NO.		3. SOLICITATION NO. 223-99-2356		4. TYPE OF SOLICITATION <input type="checkbox"/> SEALED BID (IFB) <input checked="" type="checkbox"/> NEGOTIATED (RFP)		5. DATE ISSUED	
7. ISSUED BY DHHS/PHS/FDA/OFACS/DCPM Contracts Operations Branch, HFA-512 5600 Fishers Lane, FHSL Bldg., Room 2129 Rockville, Maryland 20857 (FOR US MAIL ONLY)		CODE		8. ADDRESS OFFER TO (If other than Item 7) DHHS/PHS/FDA/OFACS/DCPM Contracts Operations Branch, HFA-512 5630 Fishers Lane, FHSL Bldg., Room 2129 Rockville, Maryland 20852		6. REQUISITION/PURCHASE NO. X24824	

NOTE: In sealed bid solicitations "offer" and "offeror" mean "bid" and "bidder".

SOLICITATION

9. Sealed offers in original and 7 copies for furnishing the supplies or services in the Schedule will be received at the place specified in Item 8, or if handcarried, in the depository located in See Block 8 until 3PM local time 8/9/99
(Hour) (Date)

CAUTION - LATE Submissions, Modifications, and Withdrawals: See Section L, Provision No. 52.214-7 or 52.215-10. All offers are subject to all terms and conditions contained in this solicitation.

10. FOR INFORMATION CALL:	A. NAME Patricia Wright	B. TELEPHONE NO. (Include area code) (NO COLLECT CALLS) (301) 827-7163
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(✓) SEC.	DESCRIPTION	PAGE(S)	(✓) SEC.	DESCRIPTION	PAGE(S)
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OFFER (Must be fully completed by offeror)

NOTE: Item 12 does not apply if the solicitation includes the provisions at 52.214-16, Minimum Bid Acceptance Period.

12. In compliance with the above, the undersigned agrees, if this offer is accepted within calendar days (60 calendar days unless a different period is different period is inserted by the offeror) from the date for receipt of offers specified above, to furnish any or all items upon which prices are offered at the price set opposite each item, delivered at the designated point(s), within the time specified in the schedule.

13. DISCOUNT FOR PROMPT PAYMENT (See Section I, Clause No. 52-232-8)	10 CALENDAR DAYS %	20 CALENDAR DAYS %	30 CALENDAR DAYS %	CALENDAR DAYS %
14. ACKNOWLEDGMENT OF AMENDMENTS (The offeror acknowledges receipt of amendments to the SOLICITATION for offerors and related documents numbered and dated:	AMENDMENT NO.	DATE	AMENDMENT NO.	DATE

15A. NAME AND ADDRESS OF OFFEROR	CODE	FACILITY	16. NAME AND TITLE OF PERSON AUTHORIZED TO SIGN OFFER (Type or print)
15B. TELEPHONE NO. (Include area code)	15C. CHECK IF REMITTANCE ADDRESS IS DIFFERENT FROM ABOVE - ENTER SUCH ADDRESS IN SCHEDULE.	17. SIGNATURE	18. OFFER DATE

AWARD (To be completed by Government)

19. ACCEPTED AS TO ITEMS NUMBERED	20. AMOUNT	21. ACCOUNTING AND APPROPRIATION
22. AUTHORITY FOR USING OTHER THAN FULL AND OPEN COMPETITION: <input type="checkbox"/> 10 U.S.C. 2304(c) () <input type="checkbox"/> 41 U.S.C. 253(c) ()	23. SUBMIT INVOICES TO ADDRESS SHOWN IN (4 copies unless otherwise specified)	ITEM
24. ADMINISTERED BY (If other than Item 7)	25. PAYMENT WILL BE MADE BY	CODE
26. NAME OF CONTRACTING OFFICER (Type or print) Harold E. Arnold	27. UNITED STATES OF AMERICA (Signature of Contracting Officer)	28. AWARD DATE

IMPORTANT - Award will be made on this Form, or on Standard Form 26, or by other authorized official written notice.

SECTION B - SUPPLIES OR SERVICES AND PRICES/COSTS

B.1 FDA 100 SECTION B - SUPPLIES OR SERVICES AND PRICE/COSTS

B.2 FDA 101 Background and Objectives

In performing the work as described in Section C-1, "Scope of Work," the Contractor shall consider the following:

A. Background:

The U.S. Army Medical Research and Materiel Command, Department of Defense, is funding this FDA conducted research to develop methods to improve bone health in young men and women in order to reduce the incidence of stress fractures during physical training and the incidence of osteoporotic fracture later in life. The study will evaluate the efficacy and safety of various types of dietary intervention to promote gain in bone mass at several skeletal sites in young Naval Academy Midshipmen.

There are two environmental factors that influence bone growth and peak bone mass, nutrition and physical activity. The risk of bone fracture is dependent on the peak bone mass achieved at skeletal maturity. Early adulthood, when rigorous military training occurs, is considered the last window of opportunity to maximize gain in bone mass. Young men and women at the U.S. Naval Academy, like other military trainees, sustain a high level of physical activity thus optimizing this major environmental influence on bone gain. Recent studies document the importance of adequate calcium intake to gain in bone mass during puberty and adolescence, but there is no clear understanding of the influence of calcium intake or other essential nutrients on bone consolidation in young adult populations. The proposed study focuses on optimizing nutritional factors to maximize gain in bone during early adulthood, which is considered a cost-effective approach to prevent stress and osteoporotic bone fracture. The hypothesis of this study challenges the current theory that adequate calcium intake is the only critical nutrition factor for bone gain and examines the effect of maximizing all the nutrients essential for both bone matrix formation and bone mineralization.

The proposed two year dietary intervention strategy involves supplementing male and female Midshipmen with calcium and specific nutrients in the form of a ready to drink fortified beverage (8 oz. cans) containing nutrients which have been identified as limited in the diet of teens and young adults and essential to bone matrix growth, strength, and mineralization. Midshipmen will be randomized to groups receiving either a calcium supplement or a placebo each day and then each group will also be randomized to receive daily either a liquid protein based supplement fortified with several essential nutrients or an

isocaloric, isonitrogenous, non-fortified placebo drink (both as ready to drink products in 8 fl. oz. containers). The placebo control drink will contain approximately the same total carbohydrate, energy, and fat content, and the same level of total nitrogen as the test product, but none of the supplemental nutrients.

The efficacy of these dietary interventions to promote gain in bone mass will be assessed by periodically monitoring changes in bone mineral content and bone mineral density of the spine, femoral neck, distal tibia and whole body measured by dual energy x-ray absorptiometry, changes in ultrasound parameters of the os calcis, and changes in resorption and formation markers of bone turnover. Possible mechanisms through which dietary intervention may impact on bone gain will be indicated by changes in calcitropic hormone levels, insulin-like growth factor-1, and changes in the urinary loss of calcium over the two year study.

B. Objectives:

To secure a total supply of 8 fluid ounce cans (or other appropriate containers) containing either a fortified liquid protein supplement (test product) and a total supply of its indistinguishable placebo control for daily use over two continuous years in a dietary intervention study involving approximately 320 United States Naval Academy Midshipmen.

B.3 FDA 103 Estimated and Allowable Cost

A. The estimated cost of this contract is \$(to be negotiated). The cost shall be subject to the provisions of "Limitation of Cost (APR 1984)" and "Allowable Cost and Payment (MAR 1997)" in Part II, Section I.

- OR -

A. The estimated cost of this contract is \$(to be negotiated). The cost shall be subject to the provisions of "Limitation of Cost (APR 1984)" and "Method of Payment - Letter of Credit (APR 1984)" in Part II, Section I.

B.4 FDA 111 Indirect Cost Rates - Educational Institutions and Non-profit Organizations with Negotiated Indirect Cost Rate Agreement

Incorporation of indirect cost rates shall be performed in accordance with the clause entitled "Allowable Cost and Payment (MAR 1997)" and either the clause entitled "Predetermined Indirect Cost Rates (AUG 1996)" or the clause entitled "Negotiated Overhead Rate - Fixed (APR 1984)" as applicable, in Part II, Section I, without further action of the Contracting Officer.

REQUEST FOR QUOTATIONS <i>(THIS IS NOT AN ORDER)</i>		THIS RFP <input type="checkbox"/> IS <input checked="" type="checkbox"/> IS NOT A SMALL BUSINESS-SMALL PURCHASE SET-ASIDE (52.219-4)		Page 14	PAGE OF PA
1. REQUEST NO.	2. DATE ISSUED 7/29/99	3. REQUISITION/PURCHASE REQUEST NO. X24823	4. CERT. FOR NAT. DEF. UNDER DDSA REG. 2 AND/OR DMS REG. 1	RATING	
5A. ISSUED BY DHHS/PHS/FDA/OFACS/DCPM Contracts Operations Branch, HFA-512, Room 2129 Rockville, Maryland 20857			6. DELIVER BY (Date)		
5B. FOR INFORMATION CALL: (Name and telephone no.) (No collect calls) Patricia Wright, (301) 827-7163/Fax (301) 827-7151			7. DELIVERY <input type="checkbox"/> FOB DESTINATION <input type="checkbox"/> OTHER (See Schedule)		
8. TO: NAME AND ADDRESS, INCLUDING ZIP CODE			9. DESTINATION (Consignee and address, including ZIP Code)		
10. PLEASE FURNISH QUOTATIONS TO THE ISSUING OFFICE IN BLOCK 6A ON OR BEFORE CLOSE OF BUSINESS (Date) 8/13/99 - 3PM		11. BUSINESS CLASSIFICATION (Check appropriate boxes) a. STANDARD INDUSTRIAL CLASSIFICATION CODE c. <input type="checkbox"/> SMALL <input type="checkbox"/> OTHER THAN SMALL <input type="checkbox"/> DISADVANTAGED <input type="checkbox"/> WOMEN-OWNED b. SMALL BUSINESS SIZE STANDARD			

IMPORTANT: This is a request for information, and quotations furnished are not offers. If you are unable to quote, please so indicate on this form return it to the address in block 5A. This request does not commit the Government to pay any costs incurred in the preparation of the submission of this quotation contract for supplies or services. Supplies are of domestic origin unless otherwise indicated by quote. Any representations and/or certifications attached to this Request for Quotations are completed by the quote.

12. SCHEDULE (Include applicable Federal, State and local taxes)

ITEM NO. (a)	SUPPLIES/SERVICES (b)	QUANTITY (c)	UNIT (d)	UNIT PRICE (e)	AMOUNT (f)
	Calicum Ginate and Placebo Tablets in Plastic Bottles (A Dietary Strategy to Maximize Bone Mass in United States Naval Academy Midshipmen)				

13. DISCOUNT FOR PROMPT PAYMENT <input type="checkbox"/>	10 CALENDAR DAYS %	20 CALENDAR DAYS %	30 CALENDAR DAYS %	CALENDAR
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NOTE: Additional provisions and representations ☐ are ☐ are not attached.

14. NAME AND ADDRESS OF QUOTER (Street, city, county, State and ZIP Code)	15. SIGNATURE OF PERSON AUTHORIZED TO SIGN QUOTATION	16. DATE OF QUOTATION
	17. NAME AND TITLE OF SIGNER (Type or print) Patricia Wright, Contracting Officer	18. TELEPHONE (Include area code)

DEPARTMENT OF
HEALTH AND HUMAN SERVICES

PURCHASE/SERVICE/STOCK REQUISITION

BPA and Call No. _____

REQUISITION NUMBER

X-24823

OFFICE CODE/SYMBOL

TO Div. of Contracts & Procurement Mgmt, OFACS (HFA-520)		REQUEST FOR <input type="checkbox"/> PURCHASE <input checked="" type="checkbox"/> SERVICE <input type="checkbox"/> STOCK ISSUE <input type="checkbox"/> RENTAL/LEASE	
REQUESTING ORGANIZATION Food and Drug Administration		CUSTODIAL AREA CFSAN	DATE 3-30-99
FOR REFERENCE CALL Juanita Pointer		EXTENSION 202-205-4098	APPROPRIATION 7590600 22390D/10
DELIVER TO Mona S. Calvo, Ph.D. (HFS-452) Office of Special Nutritionals, CFSAN 200 C Street, S.W. Washington, D. C. 20204		CAN 9-6991697-X-24823	
		DATE REQUIRED	

ITEM NO.	DESCRIPTION (INCLUDE STOCK NUMBER, MODEL/PART NO., ETC.)	QUANTITY REQUIRED	UNIT OF ISSUE	COST	
				UNIT	TOTAL
	REQUEST FOR CALICUM CITRATE AND PLACEBO TABLETS IN PLASTIC BOTTLES (A DIETARY STRATEGY TO MAXIMIZE BONE MASS IN UNITED STATES NAVY ACADEMY MIDSHIPMEN)				\$24,885.00
	PERIOD OF PERFORMANCE: May 1, 1999 to April 30, 2001				
	SOURCES: (1) Mission Pharmacal Company Neil B. Walsdorff, President P. O. Box 786099 San Antonio, TX 78278-6099 Phone 210-696-8400 FAX: 210-696-6020				
	(2) Bristol-Myers Squibb/Mead Johnson Nutritionals (R10) Robert A. Burns, Ph.D. 2400 West Lloyd Expressway Evansville, IN 47721-0001 Phone: 812-429-7987 FAX: 812-429-5925				
	(3) Celadon Dietary Supplement Corporation Robert Hesslink, Ph.D. Celadon Sciences P. O. Box 501691 San Diego, CA 92150				
	SEE ATTACHED SPECIFICATIONS				
	Funds received under IAG Number 224-98-2568				

I certify that the property/services requested are required for Government business, and are not available from excess or current assets.*		FUNDS AVAILABLE (Signature/Title) <i>[Signature]</i> Acting Leader, BEFRT		DATE 3/15/99	TOTAL \$24,885.00
REQUESTED BY (Signature/Title)* <i>[Signature]</i> Mona S. Calvo, Project Officer	DATE 3/30/99	RECEIVING OFFICIAL - I certify that the quantities indicated in the "Quantity Required" column above have been received in total or as annotated.			
RECOMMEND APPROVAL (Signature/Title)* <i>[Signature]</i> Lora A. Love, Director, CRRS, OSN	DATE 3/31/99	RECEIVING OFFICIAL (Signature/Title)*		DATE	
APPROVED BY (Signature/Title)* <i>[Signature]</i> Elizabeth A. Yetley, Director, OSN	DATE 3/31/99	ORDER NO. (PO, DO, FEDSTRIP, ETC.)		ORDER DATE	
PROPERTY MANAGEMENT OFFICER (Signature)*	DATE	VOUCHER NO.		VOUCHER DATE	

**DEPARTMENT OF
HEALTH AND HUMAN SERVICES
PURCHASE/SERVICE/STOCK REQUISITION**

BPA and Call No. _____

REQUISITION NUMBER

X24829

OFFICE CODE/SYMBOL

TO Division of Contracts and Procurement Mgmt, OFACS		REQUEST FOR <input type="checkbox"/> PURCHASE <input checked="" type="checkbox"/> SERVICE <input type="checkbox"/> STOCK ISSUE <input type="checkbox"/> RENTAL/LEASE	
REQUESTING ORGANIZATION Food and Drug Administration		CUSTODIAL AREA CFSAN	DATE 9-28-99
FOR REFERENCE CALL Juanita T. Pointer		EXTENSION 202-205-4098	OBJECT CLASS 25.38
DELIVER TO Mona S. Calvo, Ph.D. (HFS-452) Office of Special Nutritionals 200 C Street, S.W. Washington, D. C. 20204		APPROPRIATION 7590600 22390D/10	
		CAN 9-6991697-X-24829	
		DATE REQUIRED	

ITEM NO.	DESCRIPTION (INCLUDE STOCK NUMBER, MODEL/PART NO., ETC.)	QUANTITY REQUIRED	UNIT OF ISSUE	COST	
				UNIT	TOTAL
	MEMORANDUM OF NEED - NEW INTERAGENCY AGREEMENT IAG NUMBER: 224-99-2598 TITLE: Naval Academy Dietary Study (Supply of Calcium Tablets and Placebo Control Tablets) PERIOD OF FUNDING AND AMOUNT AVAILABLE FOR OBLIGATION: DISTRIBUTION OF HHS-393: HFA-520 (original pinik) HFY-1 (blue) HFA-120 (yellow) HFS-669 (pink & white) HFA-100 (yellow)				\$275,000
	Office of Financial Management _____ Date _____				

I certify that the property/services requested are required for Government business, and are not available from excess or current assets.*

FUNDS AVAILABLE (Signature/Title)

Darryl Patterson, Acting Leader, BEFPT

DATE

9/29/99

TOTAL

\$275,000

REQUESTED BY (Signature/Title)* Mona S. Calvo, Project Officer	DATE 9-28-99	RECEIVING OFFICIAL - I certify that the quantities indicated in the "Quantity Required" column above have been received in total or as annotated.	
RECOMMEND APPROVAL (Signature/Title)* Elizabeth Yetley, Director, OSN	DATE 9-28-99	RECEIVING OFFICIAL (Signature/Title)*	DATE
APPROVED BY (Signature/Title)* Extramural Resource Team	DATE 9/28/99	ORDER NO. (PO, DO, FEDSTRIP, ETC.)	ORDER DATE
PROPERTY MANAGEMENT OFFICER (Signature)*	DATE	VOUCHER NO.	VOUCHER DATE

Description of Work (continued)

The calcium citrate and placebo tablets shall be contained in a lightweight plastic bottle or suitable container (not glass) large enough to contain a month supply of tablets when four (4) tablets are consumed per day ($4 \times 31d = 124$). Each bottle shall contain one month's supply of either calcium citrate tablets or placebo tablets or no fewer than 124 tablets. There are 240 Midshipmen in the study and the tablets will be fed for two continuous years (24 months), therefore a total of 5,760 bottles are needed (2,880 of which contain calcium citrate and 2,880 of which contain the placebo).

All batches of calcium citrate tablets and placebo tablets shall be labeled with an appropriate and specific bar-coded plain white paper label. The bottles of calcium citrate shall be distinguished from bottles containing placebo tablets by placing either green or yellow colored circles on both the top and the white paper label of each respective bottle. All bottles of tablets of the same product type from all batches shall be labeled with the same color circle on the top and on the white bar-coded label. The FDA must maintain a double blind study design in this intervention study. Therefore, the identity of the calcium citrate or placebo tablets shall not be disclosed to any government personnel (FDA), except those designated at the time the products are delivered. Each container or bottle of tablets shall have the critical information pertaining to lot number, expiration date, and manufacturer's identification stamped on each bottle. The name of the manufacturer may also be printed with their address on the plain white paper label, but this information shall be identical on both product types.

The bottles of tablets shall be shipped to the FDA according to a mutually agreed upon schedule. The first shipment shall arrive no later than March 1, 2000. Subsequent shipments must be timely to meet the experimental needs of the dietary study and will be coordinated with the shipment of the protein and placebo bars.

Supplement for Naval Academy Research Calcium Study (SNARCS Bars) and Placebo Bars

The Combat Feeding Center of Natick Soldier Center shall assist FDA in optimizing the formulae and oversee and ensure the production of a total of 180,000 bars, 90,000 of which are supplemental nutrient/ protein bars (SNARCS) and 90,000 are placebo bars.

The overall guidance for the formulation used for both the test product and the placebo will be provided by the FDA with some recommendations as to the specific source materials to use and the desired final nutrient concentration. However, the FDA requires the Combat Feeding Center's expertise in final formulation and extensive experience to develop a prototype and final product for both the SNARCS and placebo bar. The FDA will also require assistance and oversight of the quality assurance and quality control aspects of the production of both product types. This specifically requires testing each batch of test product and placebo for each essential nutrient that has been identified as critical to the study design or to FDA nutrient labeling requirements (NLEA).

All bars shall be individually wrapped in plain Mylar wrappers and labeled with an appropriate and specific bar code. The SNARCS shall be distinguished from the placebo bars by placing either blue or red colored circles on each respective bar wrapper. All wrappers on bars of the same product type shall be labeled with the same color circle on the top. The FDA must maintain a double blind study design in this intervention study. Therefore, the identity of the SNARCS or placebo bar shall not be disclosed to any FDA personnel, except those designated at the time the products are first delivered. Each bar label shall be stamped with the critical information pertaining to lot number, expiration date, and manufacturer's identification. The name of the manufacturer and the developer (Combat Feeding Program Natick Soldier Center) may also be printed with their addresses on each bar wrapper, but this information shall be identical on both product types.

The SNARCS and placebo bars shall be wrapped individually in labeled Mylar wrappers and packaged in boxes containing one month supply or 31 bars of the same product type. The boxes shall be shipped to the government (FDA) according to a mutually agreed upon schedule. The first shipment shall arrive no later than March 1, 2000. Earlier shipment is strongly encouraged and consistent with the original dietary intervention schedule. Subsequent shipments must be timely to meet the experimental needs of the dietary study.

Page 3 – IAG Number 224-99-2598**Cost Estimate:**

The following cost estimates are based on past experience with the development and manufacture of similar nutrient bar products. The FDA understands that these estimates are subject to change and has several options to meet an unforeseen higher cost.

Cost of procurement of calcium supplements and placebo for entire study	<u>Estimated Amount</u> \$25,000
Cost of procurement of nutrient supplements and placebo for entire study:	
1. Production and packaging of the bars (unit cost estimate: \$1.00/bar) (No overhead rate)	\$180,000
2. Product development and formulation refinement (direct site work)	\$ 44,000
3. Analytical QA/QC work (protein sugar, fat, vitamin, mineral etc.) (Estimate based on \$1000 per analytic profile for 20 samples)	<u>\$ 20,000</u>
TOTAL ESTIMATED COSTS.....	\$269,000


ALL FUNDS WILL BE APPLIED TO A CONTRACT.

SIGNATURE PAGE


IAG NUMBER: 224-98-2568/Modification No. 2

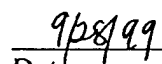
TITLE: A Dietary Strategy to Maximize Bone Mass in
United States Navel Academy Midshipmen

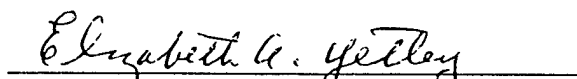
Funding Data: See Attached HHS-393
(Requisition Number X24822)

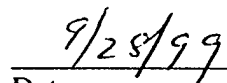

Project Officer

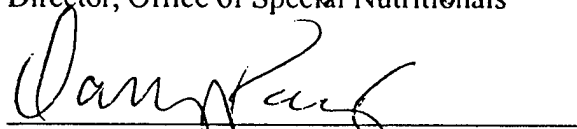
APPROVED:

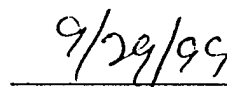

Chief, Clinical Research and Review Staff


Date

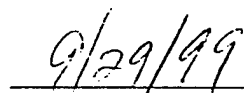

Director, Office of Special Nutritionals

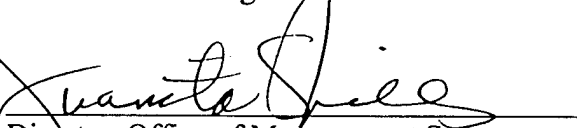

Date


Acting Leader, Budget Execution and
Fiscal Policy Team

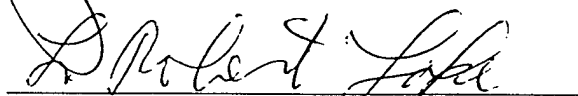

Date



Director, Division of Planning and
Resources Management


Date


Director, Office of Management Systems


Date


Director, Center for Food Safety and
Applied Nutrition


Date

Director, Office of Financial Management

Date

**MEMORANDUM REQUESTING APPROVAL OF CHANGES IN STUDY
DESIGN AND REQUEST FOR ADDITIONAL FUNDS**

DATE: 10/21/1999

TO: LTC KARL E. FRIEDL, DIRECTOR, U.S. ARMY OPERATIONAL
MEDICINE RESEARCH PROGRAM, U.S. ARMY MEDICAL RESEARCH
AND MATERIEL COMMAND, FORT DETRICK, FREDERICK, MD

CHERYL MILES, CONTRACT SPECIALIST, U.S. ARMY MEDICAL
RESEARCH AND MATERIEL COMMAND, FORT DETRICK, FREDERICK,
MD

CC: LTC KATHLEEN SHEEHAN, PROJECT OFFICER (FAX: 508-233-4195)

FROM: MONA S. CALVO, PH.D., CLINICAL RESEARCH AND REVIEW STAFF,
HFS-452, CENTER FOR FOOD SAFETY AND APPLIED NUTRITION, FDA
PRINCIPAL INVESTIGATOR, IAG NO. 17- 98- IA- 8002

RE: REQUEST FOR APPROVAL OF MODIFICATION OF STUDY DESIGN AND
DEMONSTRATION OF NEED FOR ADDITIONAL FUNDS FOR DIETARY
SUPPLEMENT PROCUREMENT

This memorandum is to request guidance and approval of needed changes to our current study design for IAG No. 17-98-8002 entitled *A Dietary Strategy to Maximize Bone Mass in U.S. Naval Academy Midshipmen*. This study examines the safety and efficacy of two different dietary supplements, fed separately or in combination over two continuous years, to increase bone mass in U.S. Naval Academy Midshipmen. The FDA openly competed both contract requests for the procurement of these dietary supplements in FY99 and received no responses. FDA then negotiated with the Combat Feeding Program at Natick Soldier Center to procure both supplements. The FDA offered an Inter Agency Agreement to Natick in order to commit funds for this procurement before the end of FY99. We were unsuccessful in establishing this IAG for FY99, but both Natick and FDA are keen to negotiate this for FY2000.

In the process of determining the feasibility of this work and the best and most cost-effective supplement type to develop for the fortified protein supplement, discussion between FDA and the experts at Natick led to the realization that the initial budget for procuring the protein supplement was insufficient. We both agreed that the best supplement form would be a fortified protein bar and placebo bar, rather than a drink as proposed originally. Natick experts predicted a problem with gel formation in the placebo drink as originally proposed. A fortified protein bar and placebo protein bar has many advantages over the proposed drink products including lower overall production cost, ease and lower cost of transportation, shorter time between development and

10/21/1999

IAG No. 17-98-IA-8002

production given Natick's experience with Hoohal bars, as well as a greater acceptability by the Midshipmen based on their current use of Power Bars.

We encountered several problems in developing the contract and present here the options that we could pursue. The cost of bar production for the proposed total number of subjects for two years exceeded the \$200,000 budgeted for this product and placebo. Natick scientists calculated additional costs of \$44,000 for product development and refinement, and \$20,000 for analytical QA/QC work to establish the needed analytical profiles. They were comfortable that the cost of the calcium supplements and placebo approximated the budgeted \$25,000. With a total line budget of \$225,000 for both types of supplements and their respective placebos, we arrived at the following options:

- 1) Request all the additional funds (\$75,000) to meet the budget over-run. Total estimated cost for 280 subjects over 2 years is \$299,000.
- 2) Reduce the subject number in each group from 35 to 30, without diminishing the power of the study to detect differences in bone mass. This would lower the cost of the bars to an estimated \$180,000, but would still require additional funds (\$45,000), since total estimated cost for 240 subjects over 2 years is \$270,000.
- 3) Reduce the feeding duration of the study from 24 months to 18 months. This would reduce the number of bars needed to an estimated 160,000, but may evoke a higher unit price and is probably too short a period of time to detect changes in bone accretion.

Natick scientists estimated that production unit costs for a total of 180,000 bars, which would be needed for two years daily intake for groups containing 30 subjects, would approximate \$1.00 per bar and for smaller total productions may approach \$2.00 per bar. In developing the IAG for FY99, we chose the second option for its cost-saving feature, and because it was closer to the reality of the number of female Midshipmen from the class of 2003 that we will be able to recruit. Enrollment of female Midshipmen was at a three year low, and to date, almost 30 women from the class of 2003 have left. If there are insufficient female subjects from the class of 2003 to meet the needed 120 total, then we propose to recruit the remainder from the youngest female Midshipmen from the class of 2002, if this meets with your approval.

We seek guidance and approval as to which of these or other options to take before we start to renegotiate this IAG for the procurement of these supplements and placebos. It is our opinion that the second option has the most advantages, if the additional cost could be met. Dr. Barton performed the power analyses for groups of 25 individuals as a safe guard against attrition (16%) and determined that this size also had sufficient power to detect differences of 4, and 6% at the three skeletal sites. In the original proposal, we presented the power estimates for group sizes of 30 which allowed for an attrition rate of 14% based on groups of 35 subjects. These power estimates are presented as they were in the original proposal in Attachment A.

Mona S. Calvo, Ph.D.

CRRS, OSN, CFSAN, FDA

Phone: 202-205-5199 FAX: 202-205-3126 E-mail: mona.calvo@cfsan.fda.gov

ATTACHMENT APOWER ESTIMATES FOR GROUP SIZES OF 30 FROM PAGE 14 OF ORIGINAL PROPOSAL:

For this study, we considered an increase in bone density of approximately 4 to 6% (depending on the skeletal site) in those participants whose physical activity and nutrient intake is optimized over two years as evidence that the proposed dietary intervention strategy is effective in maximizing gain in bone mass. Previous bone densitometry measures in 79 healthy female Midshipmen with a mean age of 18.4 years at entry showed 1.8% gain at the femoral neck, 2.6% gain at the lumbar spine, a 3.4% gain at the tibia and a 4.6% gain in total body mineral content (TBMC) over two years (78). A similar study in 44 healthy male Midshipmen with an average age of 18.8 years at entry showed a 2.3% gain at the femoral neck, a 4.1% gain at the lumbar spine and tibia and a 10.4% increase in TBMC over 4 years (79).

Statistical power analyses were performed for an analysis of covariance design (with a baseline bone density as the covariate) using mean and variability estimates from cross-sectional data from the Naval Academy class of 1996 and 1998. Powers were computed for the main effects of calcium intake or mineral and vitamin intake in a three-factor design with calcium intake, mineral and vitamin intake, and sex as the three factors. Because bone density should not vary greatly within an individual over a two year period, we assumed a 0.7 within-subject correlation between the baseline and final measurement. Powers were computed for detecting differences of 2, 4, and 6 percent in final bone density. A sample size of 30 per group was used, which allows for a 14 percent attrition over two years. For femoral neck, the powers were 0.39, 0.92, and 0.999 for 2, 4, and 6 percent differences. For tibia, the powers were 0.59, 0.99, and 1.00 for 2, 4, and 6 percent differences. For total body mineral content, the powers were 0.38, 0.91 and 0.998 for 2, 4, and 6 percent differences.

If needed, we can submit similar power estimates for group sizes of 25 which demonstrate sufficient power with an attrition rate of 16% for the proposed group size of 30.



Memorandum

Date 07/14/99

From Chemist, Clinical Chemistry Unit,
Beltsville Technical Operations Staff, CFSAN, HFS-025

Subject Cost estimate for study entitled "A Dietary Strategy to Maximize Bone Mass in United States Naval Academy Midshipmen"

To Mona Calvo, Ph. D., Clinical Research and Review Staff, OSN,
CFSAN, HFS-452

As per your request, the Clinical Chemistry Unit has estimated the costs to analyze five sets of 320 samples. A set of 320 samples would be analyzed every 6 months for 2 and a half years. The cost per set of 320 samples is listed below per instrument.

1) **Dimension AR**

Analytes: sodium, potassium, chloride, calcium, phosphate, magnesium, BUN, creatinine, ALP, total protein, albumin, and uric acid in serum or plasma.

sodium, potassium, creatinine, calcium and phosphate in urine

Estimated cost per set of 320 samples: \$2,463.33

2) **Coulter S+IV**

Analytes: hematology (WBC, RBC, Hgb, HCT, MCV, MCH, MCHC, RDW, and PLT)

Estimated cost per set of 320 samples: \$544.07

3) **Ferrochem II**

Analytes: iron and total iron binding capacity

Estimated cost per set of 320 samples: \$1,435.30

4) **Nova 7+7**

Analytes: total calcium, ionized calcium, pH, and normalized calcium

Estimated cost per set of 320 samples: \$264.40

The cost for each set of 320 samples is \$4,707.10 and the total cost for all five sets of samples is \$23,535.50.

If you have any questions about the cost estimate, please contact me at (301) 594-5003.

Cheryl Ford
Cheryl Ford

cc: Juanita Pointer, HFS-669
Marie Nolte, HFS-667

STUDY NO. BFO- -

CFSAN/OSC/BTOS/CLINICAL CHEMISTRY UNIT (CCU)

SUPPORT PROTOCOL

SUPPORT REQUESTED DATE: 04/09/99

SUPPORT COMPLETION DATE:

SUPPORT ACTIVITY FOR THE STUDY UNIT: Clinical Research and Review Staff, OSN, CFSAN

SUPPORT PROTOCOL TITLE: Quantitation of Specified Clinical Parameters in human serum and urine, and specified hematological parameters in human whole blood for the study entitled "A Dietary Strategy to Maximize Bone Mass in United States Naval Academy Midshipmen".

OBJECTIVE: To determine the contents of specified Clinical parameters (Na, K, Cl, CA, phosphate, MG, BUN, CREA, ALP, TP, ALB, IRN, TIBC, URCA and possibly ionized calcium) in human serum samples, specified clinical parameters (Na, K, Cl, CA, CREA, and phosphate) in human urine samples, and specified hematological parameters (WBC, RBC, Hgb, Hct, MCV, MCH, MCHC, RDW, and PLT) in human whole blood samples in support of the study entitled "A Dietary Strategy to Maximize Bone Mass in United States Naval Academy Midshipmen", Monica Calvo, Ph.D., Principal Investigator.

EXPERIMENTAL DESIGN: Approximately 320 serum samples, 320 urine samples, and 320 whole blood samples will be collected every 6 months for two and a half years. A maximum of 60 samples will be collected per day. Samples may be transferred in their original containers. Sample transfer will be documented on CCU RECORD FORM #1. Whole blood samples should be placed in vacutainers according to the table below.

Analytes	Vacutainer Top Color	Number of Tubes	Amount Required
Ionized CA	red top	1	2mL
Clinical	red top	1	2mL
Hematological	lavender	1	0.75 mL

Samples in red top tubes should be gently inverted 5 times and then allowed to clot for 30 minutes. Samples in lavender top tubes should be mixed gently. Analysis of hematological parameters must be completed within 24 hours of collection.

After receipt of each set of samples, the samples will be handled following CCU-SOP#1-revision 6.

Each set of samples will be analyzed for the requested analytes as follows:

ANALYTES	INSTRUMENT	CCU-SOP No.
Clinical	Dimension AR	2 - rev. 2
Hematological	Coulter S+IV	28 - rev. 7
Iron & TIBC	Ferrochem II	29 - rev. 1
total & ionized CA	Nova 7 + 7	30

DEPARTMENT OF
HEALTH AND HUMAN SERVICES

PURCHASE/SERVICE/STOCK REQUISITION

BPA and Call No. _____

REQUISITION NUMBER

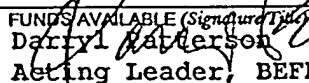
X24825

OFFICE CODE/SYMBOL

TO Division of Contracts & Procurement Mgt.		REQUEST FOR <input type="checkbox"/> PURCHASE <input checked="" type="checkbox"/> SERVICE <input type="checkbox"/> STOCK ISSUE <input type="checkbox"/> RENTAL/LEASE	
REQUESTING ORGANIZATION Food and Drug Administration		CUSTODIAL AREA CFSAN	DATE 7/21/99
FOR REFERENCE CALL Juanita T. Pointer		EXTENSION 205-4098	APPROPRIATION 7590600 22390D/10
DELIVER TO Mona S. Calvo, Ph.D. (HFS-452) Office of Special Nutritionals 200 C Street, S.W. Washington, D.C. 20204		CAN 9-6991697-X-24825	
		DATE REQUIRED	

ITEM NO.	DESCRIPTION (INCLUDE STOCK NUMBER, MODEL/PART NO., ETC.)	QUANTITY REQUIRED	UNIT OF ISSUE	COST							
				UNIT	TOTAL						
	<p>Memorandum of Need-NEW Interagency Agreement</p> <p>IAG Number: 224-99-2586</p> <p>Title: Bone Mineral Density Determinations (A Dietary Strategy to Maximize Bone Mass in United States Naval Academy Midshipmen)</p> <p>Period of Funding and Amount Available for Obligation</p> <p>Distribution of HHS-393:</p> <table><tr><td>HFA-520 (original pink)</td><td>HFY-1 (blue)</td></tr><tr><td>HFA-120 (yellow)</td><td>HFS-699 (pink & white)</td></tr><tr><td>HFA-100 (yellow)</td><td></td></tr></table> <p>Director, Office of Financial Management</p>	HFA-520 (original pink)	HFY-1 (blue)	HFA-120 (yellow)	HFS-699 (pink & white)	HFA-100 (yellow)					\$28,300
HFA-520 (original pink)	HFY-1 (blue)										
HFA-120 (yellow)	HFS-699 (pink & white)										
HFA-100 (yellow)											

I certify that the property/services requested are required for Government business, and are not available from excess of current assets.*

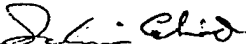

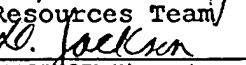
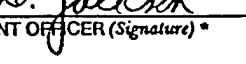
FUNDS AVAILABLE (Signature/Title)

 Darrell Patterson
 Acting Leader, BEFPT

DATE

7/20/99

TOTAL

\$28,300

REQUESTED BY (Signature/Title)* Mona Calvo P.O. 	DATE 7-25-99	RECEIVING OFFICIAL - I certify that the quantities indicated in the "Quantity Required" column above have been received in total or as annotated.	
RECOMMEND APPROVAL (Signature/Title)* Elizabeth Yetley Director, OSN 	DATE 7/23/99	RECEIVING OFFICIAL (Signature/Title)	DATE
APPROVED BY (Signature/Title)* Extramural Resources Team 	DATE 7/26/99	ORDER NO. (PO, DO, FEDSTRIP, ETC.)	ORDER DATE
PROPERTY MANAGEMENT OFFICER (Signature)* 	DATE	VOUCHER NO.	VOUCHER DATE



DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

Page 27



INTERAGENCY AGREEMENT

1. IAG NO. (FDA) 224-99-2586		2. TYPE OF AGREEMENT <input checked="" type="checkbox"/> New <input type="checkbox"/> Mod <input type="checkbox"/> Administrative <input type="checkbox"/> No Cost Ext.		3. MODIFICATION NO.	
4. TITLE OF PROJECT Bone Mineral Density Determinations (A Dietary Strategy to Maximize Bone Mass in U.S. Naval Academy Midshipment)					
5. DESCRIPTION OF WORK - ATTACHED			6. AMOUNT \$28,300		
7. NAME AND ADDRESS OF PARTICIPATING FEDERAL AGENCY Office of Naval Research (Code 341) 800 North Quincy Street Arlington, Virginia 22217			LIAISON NAME: CDR Douglas Forcino Program Officer		PHONE NO. (703) 696-0367 Fax 703-696-1217
8. NAME AND ADDRESS OF PARTICIPATING FDA UNIT CFSAN/Office of Special Nutritionals 200 c Street, S.W. Washington, D.C. 20204			LIAISON NAME: Mona Calvo, Ph.D.		PHONE NO. (202) 205-5199
9. PERIOD OF AGREEMENT FROM 7/1/99 THROUGH 9/30/99					

This agreement may be terminated by either party upon a thirty day advance written notice.

10. AUTHORITY (FDA) <input type="checkbox"/> Economy Act approved June 30, 1932, as amended by 31 U.S.C. 1535 <input checked="" type="checkbox"/> Section 301 of the Public Health Service Act (42 USC 241) <input type="checkbox"/> Other (specify) _____		11. AUTHORITY (Other Agency)	
12. FDA FUNDING INFORMATION 7590600 22390D/10 9-6991697-X-24825 <input checked="" type="checkbox"/> Increase from 0 by \$28,300 to \$28,300 <input type="checkbox"/> Decrease from _____ by _____ to _____			
13. Administrative billing requirements will comply with GAO Policy and Procedures, Title 7, Section 8.4 <input checked="" type="checkbox"/> Billing: X OPAC system FDA ALC 75060099 Other Agency ALC _____ <input type="checkbox"/> SF 1080 - FDA Accounting (HFA-120) 5600 Fishers Lane, Rockville, MD 20857			
14. PARTICIPATING AGENCY FUNDING INFORMATION (This block must be completed if funding is being provided to the FDA) a. Legal authority for the acquisition of supplies/services exists within your agency. b. This action does not conflict with any other agency's authority or responsibility			
15. PARTICIPATING AGENCY IS <input checked="" type="checkbox"/> Required to sign <input type="checkbox"/> Not required to sign			
16. FDA ACCEPTANCE NAME: Rosemary Springer TITLE: Senior Grants Management Specialist, OFACS DATE: _____		17. PARTICIPATING AGENCY ACCEPTANCE NAME: _____ TITLE: _____ DATE: _____	

INTERAGENCY AGREEMENT NUMBER 224-99-2586

Title: Bone Mineral Density Determinations (*A Dietary Strategy to Maximize Bone Mass in United States Naval Academy Midshipmen*)

Background:

In FY 1998, FDA received funds from the U.S. Army Medical Research and Materiel Command, Department of Defense to conduct research to develop methods to improve bone health in young men and women in order to reduce the incidence of stress fractures during physical training and the incidence of osteoporotic fracture later in life.

Scope of Work:

Through a third-party arrangement, the Office of Naval Research will have the determinations supervised by the Co-Principal Investigator, Dr. David Armstrong, of Bethesda Naval Hospital and the medical monitoring of this task will be carried out by CAPT. Robert Schultz, USN MC, of the Naval Clinic at Annapolis, MD. He will be working with approximately 320 Naval Academy Midshipmen (Class of 2003), using the dual energy-X-ray absorptiometer (DEXA, Norland XR-36) measurement (at baseline and years one and two) of bone mineral density (BMD) and bone mineral content (BMC) for the total body and at five skeletal sites including the femoral neck, trochanter, Ward's triangle, lumbar spine, and distal tibia.

Each scan includes anthropometric measures conducted at the time of each DEXA scan by a trained and experienced technician for each subject participating in the study. These measurements include height using a calibrated stadiometer, weight using a calibrated electronic scale, body composition by skin fold using Lange caliper and body girth measurements using a precise tape measure. Dependent upon the availability of a dedicated ultrasound machine located adjacent to the DEXA or Norland XR-36, the technician will also perform standard ultrasound determinations (BUA, SOS and combined measure of stiffness) immediately after each DEXA screen. The technician will also administer a simple pregnancy test (urine indicator) immediately prior to each bone scan in all participating females Midshipmen. Results of these tests will be maintained in strict confidence, but no DEXA scans will be performed in women with a positive pregnancy test.

To maintain full and complete privacy for each subject participating in the study collected data measures will be reported directly and electronically only to the study biostatistician, Dr. Curtis N. Barton, located at 200 C St. S.W., Washington, D.C.

Annual reports demonstrating quality control monitoring of the DEXA and ultrasound measures will be made to the Mona Calvo, Ph.D., Principal Investigator, 200 C Street, S.W., Washington, D. C. 20203. No other deliverables or reports are anticipated.


Estimated Cost: \$28,300

SIGNATURE PAGE

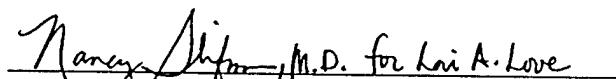
IAG Number: 224-99-2586

Interagency Agency Title: Bone Mineral Density Determinations (A Dietary Strategy To Maximize Bone Mass in United States Naval Academy Midshipmen)

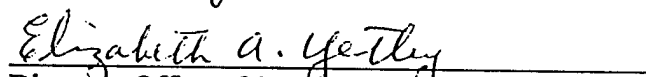
Funding Data: See Attached HHS-393
(Requisition Number X24825)


Project Officer

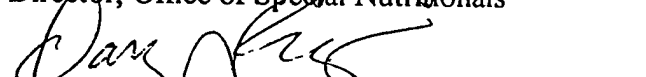
APPROVED:


Chief, Clinical Research and Review Staff


7/23/99
Date


Director, Office of Special Nutritionals


7-23-99
Date


Acting Leader, Budget Execution and Fiscal Policy Team


7/26/99
Date


Director, Division of Planning and Resources Management

7/27/99
Date


Director, Office of Management Systems

7/27/99
Date


Director, Center for Food Safety and Applied Nutrition

7-27-99
Date

Director, Office of Financial Management

Date